



Application of

Joel R. Studin

Serial No.

10/829,315

Filed

April 21, 2004

Examiner

Sheikh, Humera N.

Art Unit

1615

Title

Method and Composition for the Treatment of Scars

Commissioner of Patents and Trademarks P.O. Box 1450

Alexandria, VA 22313-1450

#### DECLARATION OF JOEL R. STUDIN UNDER 37 C.F.R. §1.132

I do hereby declare as follows:

- 1. THAT I received a Bachelor of Science in General Science and Psychology from the University of Rochester, Rochester, NY, in 1975.
- 2. THAT I received a Doctor of Medicine from Mount Sinai Hospital, New York, NY, in 1982.
- 3. THAT I have practiced as a Plastic and Reconstructive Surgeon since 1987.
- 4. THAT I am the inventor of the above-identified application, that I am familiar with the above-identified application, the Office Actions and applied references rendered to date.
- 5. Exhibit A is a testing report received from Bryce RX Laboratories, Inc., detailing the results of transdermal affect testing conducted by Bryce. I authorized Bryce RX Laboratories Inc. to undertake the transdermal affect testing. All dates and extraneous information have been redacted from Exhibit A.
- Exhibit A reports the transdermal effectiveness evaluation of various possible carriers for delivering topical treatments including corticosteroids for scar tissue, psoriasis, eczema and other cutaneous maladies.

  Transdermal effectiveness was determined by the well-known McKenzie-Stoughton vasoconstriction assay. The McKenzie-Stoughton assay is a skin-blanching test. Under this assay a test sample containing a carrier and hydrocortisone was applied to a test subject's skin and the degree of skin blanching was observed. In accordance with the test, hydrocortisone

adsorbed into the skin causes a localized vasoconstriction at the site of application of the test sample. This vasoconstriction causes the skin to appear white. The more hydrocortisone that was adsorbed into the skin, the whiter the localized spot appeared. At 1, 2, and 4-hour time intervals an observer assessed the amount of skin blanching on a scale of 0 (least blanching) to 4 (most blanching). After all data had been collected from three different observers, the scores were added up to give a total blanching score. The higher the score, the higher the level of blanching, and thus, the higher the level of hydrocortisone adsorbed into the skin.

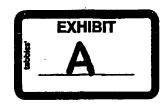
- 7. Exhibit A, page 1, provides further details for the preparation of the samples tested, and testing of those samples. Briefly, 50 ml of a carrier was added to a 200 ml beaker. 1 gm of hydrocortisone was added to the beaker and mixed until fully dissolved. Water was then added to a final volume of 100 ml. According to page 1, a 0.3 cc aliquot of each mixture was placed onto a subjects forearm and marked with a sharpie. Blanching was then observed at 1, 2, and 4-hour time intervals, and vasoconstriction was assessed on a scale of 0 (least blanching) to 4 (most blanching).
- 8. Exhibit A, pages 2-5, provides the blanching results from three observers at 1, 2, and 4-hour time intervals on four different test subjects for each carrier tested. Page 6 provides the cumulative score for each carrier tested for all four test subjects. As can be seen from page 6, Nitrocellulose (Flexible Collodion) had the highest test score (141), which indicates the greatest degree of blanching, and thus, the highest degree of transdermal transmission of the active agent (hydrocortisone) tested.
- 9. Exhibit A, page 6, also provides blanching results for methyl cellulose (14), hydroxymethylcellulose (25), nitrocellulose (flexible collodion/xanthan gum) (59), hydroxyethylcellulose (29), cellulose acetate (23), propylene glycol (7), aluminum hydroxide (49) and tragacanth (3). As can be clearly see from these results nitrocellulose showed very strong transmission of the active agent (hydrocortisone) into the test subject's skin.

10. I further declare that all statements made herein to my knowledge are true and that all statements made on information and belief are believed to be true: and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements so made may jeopardize the validity of the document, or application, or any patent issuing therefrom.

Respectfully submitted.

3/21/08 Date

Joel R. Studin



Bryce RX Laboratories, INC. DEA BB5460706

""" TESTING REPORT """

Formula: Scar/Ecz/Psoriasis

Client: Dr. Joel Studin

TRANSDERMAL AFFECT TESTING SCAR/ECZ/PSORIASIS - DR. STUDIN

The goal of this testing is to ascertain the relative efficacy of a number of possible carriers for delivering topical treatments including corticosteroids for scar tissue, psoriasis, eczema and other cutaneous maladies.

--- - METHOD / PROCESS---------

Transdermal effectiveness evaluation to be performed using the Coleman, Kanfer and Haigh method of the McKenzie - Stoughton vasoconstriction assay.

- 1. Place 50 ml of carrier into a 200ml beaker
- 2. Place igm hydrocortisone into beaker
- 3. Mix until fully dissolved or evenly dispersed
- 4. QS to 100ml
- 5. Seal beaker with plastic wrap
- 6. Repeat for all carriers.
- 7. Place digot aliquot of each mixture on flexor surface of subject forearm and mark with
- 9. Subject to wear short sleeves and avoid washing or sweating
- 9. Observe at 1,2 and 4 hours
- 10. Chart observation of skin blanching by subject and z observers
- 11. Vasoconstriction assessed on a scale of zeroxleast blanching to 4=most blanching

\*\*\*\* THIS TESTING IS A TRADE SECRET OF BRYCE RX LABORATORIES, INC. \*\*\*\*

Methyl Cell	.ulose					•		•	
Observation	1 1	1hr_	1	zhr	o '	4hr	ę ·		
	1 2								
Subject		lhr	0	zhr_	0	4hr	ିନ	_Total	Scorea
Hydrosymeth	ylcellulose								
	ı 1	ıhr	1	2hr	ı	ahr	1		
	1 2								
Subject	#1	nhr_	@	zhr_	Ø	4hr_	Ø	_ _Total	Score <u>5</u>
Nitrocellul	Lose (Flexible	Collod	ion)						
Observation	1	1hr_	4	2hr_	4_	4hr_	4	_	
Observation	1 2	1hr_	4		4	4hr	4	_	
Subject	#1	ahr_	3	ahr_	4	4hr_	4	_Total	Score <u>35</u>
Nitrocellu	lose (Flexible	Collod	ion /	' Xanth	an Gu	am )			
·· <del>-</del>	1 1	_						_	
	) <u>2</u>								
Subject	#1	1hr_	2	ahr_	2	4hr_	_1	_Total	Score <u>14</u>
Hydroxyethy	ylcellulose								•
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	1 <u>2</u>								
	#1								Score <u>z</u>
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	n <u>2</u>								
Subject	#3	ahr_	g.	zhr_	0	4hr_	a	Total	Score <u>a</u>
Propylene (	Glycol								
Übservatio	າ i	1hr_	1	2hr_	0	4hr_	ด	_	
	n <u>2</u>								
Subject	#1	nhr_		ehr_	8	4hr_	<u> </u>	_Total	Score_2
Aluminum H	ydroxide								
Observation	n 1	1hr_	2	zhr_	2	4hr_	2	_	
Observatio	n <u>z</u>	ihr_	2	zhr_	_ 1	4hr_	1	_	
Subject	#1	1hr_	2	shr	_1_	4hr_	1	_Total	Score14
Tragacanth									
	n 1								
Observatio	n <u>e                                     </u>	ahr_	ହ	zhr_	Ø	4hr_	9	_	
Subject	#1	1hr_	0	:zhr_	•	4hr_	8	_Total	Score o

Methyl Cellulose					•		
Observation 1	1hr_	_1	ahr_	_ <u>i</u> _	4hr	1	
Observation 2	1hr_	2	zhr	3.	4hr	୍ ବ	
Subject #2	a.hr_	_1_	zhr_	ହ	4hr_	Ø	Total Score7
Hydroxymethylcellulose							
Observation 1	zhr_	2_	zhr_	_1_	4hr	1	<u> </u>
Observation g	ihr_	1	zhr_	0	4hr_	Ø	<del></del> -
Subject #2	ihr_	1	ehr_	0	4hr_	0	Total Score <u>_6</u>
Nitrocellulose (Flexible	e Collod	ion)	•				
Observation 1			shr_	4.	4hr_	4	
Observation 2	ւիբ	4	2hr	d	_4hr	_4	·
Subject #2	zhr_	4	zhr_	4	4hr_	2	Total Score_ <u>SS</u>
Nitrocellulose (Flexibl	e Collod	ion /	Xanth	an G	um)		
Observation 1						1	<u>:</u>
Observation 2							
Subject #2	1hr_	2	ehr_	0	4hr_	0	Total Score10
Hydroxyethylcellulose							
Observation 1	ihi	2	zhr	2	4hr_	_1	
Observation <u>s</u>	inr_	1,	ehr	1	4hr_	ø	<u> </u>
Subject #2	ւիւչ_	<b>1</b>	zhr_	e_	4hr_	0	Total Soore <u>8</u>
Callulose Acetate		=					
Observation 1	ihr	1	ehr)	ø	4hr_	0	
Observation <u>s</u>	ahr.	<b>1</b>	zhr_		4tir	Ç.	
Subject #2	1hr_	<u> </u>	2hx_	٥	4hr_	Ø	Total Score 4
Propylene Glycol							,
Observation 1	1hr	1	shr_	8	4hr_	8	
Observation <u>a</u>	iter	1	ehr_	ø	4hr_	0	
Subject #2	ihr	0_	zhr_	ø	4hr_	<u>o</u>	Total Score <u>2</u>
Aluminum Hydroxide							
Observation 1	ahr.	- 3	zhr_	2	4hr_	(3)	
Observation <u>2</u>	ahr_		2hr_	2	4hr_	0	
Subject #2	1hr_	2_	zhr_		4hr_	<u> </u>	Total Score <u>13</u>
Tragacanth							
Öbservation 1	1hr_	0	2hr_	ø	4hz_	C	_ <del></del>
Observation <u>z</u>	1h૪_	Ø	zhr_	ø	4hr_	O	
Subject #2	zhr.	<u> </u>	zhr	. 0	4hr_	0	Total Score <u>1</u> _

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Methyl Cellu	lose				•	÷		. •
Übservation	1	1hr_	1	zhr_	Ø	4hr <u>_</u>	<u> </u>	_
Observation	2	1hr_	1	zhr_	ı	4hr c	3	_
Subject #	is	1hr_	9	shr_	0	4hr	3	_Total Score <u> </u>
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Hydroxymethy	/lcellulose						•	
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Observation	2	ıhr_	1	zhr_	1	4hr	<u>.                                    </u>	_
Subject #	‡3	ıhr_		zhr_	ହ	4hr	<i>d</i>	Total Score <u>7</u>
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	ose (Flexible							
Observation	1	1hr_	4	sur_	4	4hr	1	-
Observation	2	1hr_	4_	2hr_	4	4hr	4	<b>-</b>
Subject f	‡3	1hr_	4	shr_	4	4hr	4	_Total Score <u>-96</u>
Nitrocellul	ose (Flexible	Collod	ion /	. Xanth	on Ci			•
	1						7	
Observation	2		<del>.</del>			#!!#	<del>*</del>	-
subject (	<u>-</u>			E: IE	á	4! 1 <i>&amp;</i>		_10.63T %cot#
Hydroxyethy:	loellulose							
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	2							
Subject t	#3	ihr_	2	zhr_	_1_	4hr	9	
-								<del></del>
Cellulose Ad	petate							
Observation	1	ihr_	2	zhr_	1	4hr	0	_
Observation	2	lhr	2_	zhr	ı	4hr_	ð	
Subject (	# <sub>3</sub>	ihr_	2.	2hr_	0	4hr	ଚ	Total Scorez
•								
Propylene G	lycol							
Übservation	1	1hr_		2hr_	ø	4hr	<u> </u>	
Observation	2	1hr_	3	ahr_	1	4hr	ଚ	_
Subject :	#s	zhr_	1	2hr_	Ø	4hr	ପ	_ _Total 5core <u>4</u>
Aluminum Hy						•		,
	1							
Subject (	<b>*</b> 3	lhr_	2	zhr_	_1_	4hr	1	_Total Score <u>11</u>
Tragacanth		••						•
Observation	·	ahr	ė.	shr		4hr	e.	•
Observation	3	1 hr	1	 2hr	ø.	7'' ∡hr	<del>ට</del>	
Subject	#2		. <del></del>				6	- Total Score :

Methyl Cell	uloco			•				
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Observation	· 호		<u>.</u>	KI 1.5	<del>- 4</del> 1			<del></del>
		ınr_			- 4	4'''*		Total Scorez
Subject	#4	1111	1		ığ	AIIE	<u> </u>	
Hvdronvmeth	nylcellulose						•	
	1 1	ihr	2	201	2	4hr_	1	
Observation	1 <u>2</u>	ıhr_	3.	ehr	ı.	4hr	1	<del></del>
Subject	#4	1hr_	Ċ	ahr_	ø	4hr_	0	Total Score _7
Nitropellul	lose (Flexible	Collod	ionl					
	1 1			anr	A	ahr	<b>A</b>	•
Observation	) <u>2</u>		4	ahr	.4	45°	4	·
Subject	#4		<del></del>	202 202	4	ahr	4	
240,120 (	"1						**	
Nitrocellul	Lose (Flenible	Collod	ion /	Xanth	an G	<b>цн)</b>		•
Observation	n 1	ihr_	2	2hr_	_l	4hr_	1	
Observation	٦ <u>2</u>		2_	2hr_	2	4hr	1	· ·
Subject	#4		3	2hr_	_2_	4hr_	_1	Total Score <u>_15</u>
Hudrauusth	ylcellulose							
	1 1	abe	_	ehr		alix	a	
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Cellulose (	Acetate							
Übservatio	n 1	ihr_	_ 1	ahr_	1	4hr_	O	
	n <u>e</u>							
Subject	#3	1hr_	_1_	zhr_	1	4hr	٦	Total Score <u>8</u>
Propylene.	Glycol							
	n 1	1.hr	0	ehr	ø	abr	a	·
Observation	n <u>e </u>		Ø.	2hr	<u> </u>	abr	6	
Subject	#4	ihr_	1	shr_	0		0	Total Score <u> </u>
<b>.</b>								
Aluminum H		_ <b>L</b>	_		_		_	
	n 1							
Ubservation	n <u>2                                    </u>	ı'nr_	_3_	shr_	2	4ħr_	<u> </u>	
Subject	#4	1hr_	3	zhr_		4hr_	<u> </u>	Total Score11
Tragacenth								
Observation	n 1	1hr_	- 2	źhr_	· Ø	4hr_	0	<u> </u>
	n <u>2</u>	ahr_	9	zhr_	Q	4hr_	Ø	<del></del>
Subject	#4	1hr_	<u> 1</u>	zhr_	0	4hr_	٠	Total Score <u>l</u>

#### BASE CARRIER CUMULATIVE TOTAL SUBJECTS 1-4 (1HR, 2HR, 4HR)

Methyl Cel	lulose	
Subjects	#1-4	· Total Score 14
Нудгохужет	hylcellulose	
Subjects	#1-4	Total Score25
Nitrocellu	lose (Flexible	Collodion)
Subjects	#1-4	Total Soore 141
Nitrocellu	ulose (fléxible	Collodion / Xanthan Gum)
Subjects	#1~4	Total Score
Hydroxyeth	nylcellulose	
Subjects	#1-4	Total Score 29
Cellulose	Acetate	
Subjects	#1-4	Total Score <u>23</u>
Propylene	Glycol ·	
Subjects	#1-4	Total Score
Aluminum H	Hydroxide	'
Subjects	•	Total Score 49
Tragacanti	h	
Subjects		Total Score 3

#### Conclusion

Most carriers showed very poor transdermal transmission of the active. Nitrocellulose however, showed a very strong transmission in our formulation. We believe that this is a result of increased bio-electric binding. It is our suggestion that you continue the development of your products using the nitrocellulose base that you suggested.

**Atty. Docket No.:** SDF 04-15 **Application Serial No.:** 10/829,315

# X RELATED PROCEEDINGS APPENDIX NONE.